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(54) **ELECTROSPRAY APPARATUS FOR PRODUCING UNIFORM SUBMICROMETER DROPLETS**

**ELEKTROSPRÜHVORRICHTUNG ZUR ERZEUGUNG EINHEITLICHER SUBMIKROMETER TRÖPFCHEN**

**APPAREIL ELECTRO-ATOMISEUR PRODUISANT DES GOUTTELETTES UNIFORMES D'UNE TAILLE INFERIEURE AU MICRON**

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## Description

## BACKGROUND OF THE INVENTION

- 5    **[0001]** The present invention relates to analytical devices for detecting and characterizing minute particles and macromolecules suspended or dissolved in liquid samples, and more particularly to a means for generating droplets of the liquid samples, of a size and uniformity to enhance the effectiveness of such analytical devices.
- [0002]** The ability to analyze liquid solutions is becoming increasingly important in a wide variety of fields including medicine, pharmaceuticals, production of polymers, paints and dyes, environmental science and genetics. A variety  
10 of techniques including atomic absorption spectrometry, atomic emission spectrometry, inductive coupled plasma, light scattering, and mass spectrometry, are used to detect, characterize and determine concentrations of solutes, suspensions and residue in liquid solutions. In connection with these techniques, it is highly preferred to convert the liquid sample into aerosol form, typically by using a nebulizer.
- [0003]** While various types of nebulizers are known, including ultrasonic, pneumatic, frit and thermospray, an electro-spray nebulizer is preferred in many applications due to its ability to generate small and uniform droplets, and in its  
15 relatively high efficiency, in terms of sample droplets delivered to a detector as compared to the sample uptake rate.
- [0004]** In the electrospray nebulizer, electrically conductive liquid is supplied at a controlled rate to a capillary tube. A voltage differential between the capillary tube and a surrounding chamber wall creates an electrostatic field that induces a surface charge in liquid emerging from the tube. Electrostatic or "Coulomb" forces disperse the liquid into a  
20 fine spray of charged droplets. To produce the spray, each droplet is charged near the Rayleigh limit (at which point electrostatic repulsion overcomes surface tension).
- [0005]** When analyzing macromolecules, colloids or other small particles of interest, the particles are dispersed in a liquid, the liquid is sprayed in small droplets, then the droplets are dried, leaving the particles in aerosol form. An exemplary use of an electrospray nebulizer is disclosed in US-A-5 076 097. An apparatus for measuring concentrations  
25 of macromolecules and colloids in a liquid sample, uses an electrospray atomizer to receive a liquid analyte, after separation by a liquid chromatography system. Within the atomizer, an electrical field charges the liquid emerging at the tip of a needle, whereby the liquid is dispersed into a fine spray of charged droplets. As solvent evaporates from each droplet, charge density on the droplet surface increases until the Rayleigh limit is reached. The resulting instability causes the droplet to disintegrate into smaller droplets. The aerosol output of the electrospray atomizer is provided to  
30 a condensation nucleus counter, either directly or through diffusion screens that filter smaller particle sizes.
- [0006]** Even "pure" liquids contain some non-volatile material. Accordingly, each droplet contains a proportion of a residue, and further may contain one of the particles under study. The particle concentration in the liquid sample, and the volume of the droplets as initially formed, are kept to a minimum to avoid production of "clusters" (droplets containing two or more of the particles under study).
- 35    **[0007]** The size of residue particles depends upon residue concentration and initial droplet size. For example, a one part per million impurity level results in a residue particle of about one percent of the diameter of the original droplet (assuming the dried material and the liquid have approximately the same density). Thus, a nebulizer producing droplets 10 micrometers in diameter would produce residue particles having a diameter of about 100 nanometers.
- [0008]** Such residue particles are inconsequential, so long as particles under study are relatively large. However,  
40 residue particles cause substantial interference or artifacts that interfere with detecting and characterizing smaller particles. In many of the abovementioned fields, there is a strong interest in studying particles as small as three nanometers in diameter, e.g. macromolecules and colloids such as synthetic polymers, proteins, viruses and particles of concern in connection with maintaining semiconductor production facilities. To reduce residue artifacts, it is necessary either to reduce the non-volatile impurity concentration, or to generate smaller droplets.
- 45    **[0009]** Given the difficulty in producing and handling ultra pure liquids, generating smaller droplets appears to be the logical solution. However, the Coulomb forces employed to generate droplets also cause droplet disintegration shortly after formation. More particularly, as liquid evaporates from the droplets, surface charge density on the droplets increases until the Rayleigh limit is reached, at which point the Coulomb repulsive force becomes the same order as cohesive forces such as surface tension. The resulting instability causes the original droplet, sometimes referred to as  
50 the parent or primary droplet, to disintegrate into smaller droplets. The primary droplet appears to eject several small droplets, removing a substantial proportion of the total charge. The parent droplets and fragments continue to evaporate and can experience further fragmentations. The resulting distribution of droplet sizes is broad, i.e. non-uniform.
- [0010]** Therefore, it is an object of the present invention to provide a device for generating uniform droplets having diameters of less than one micrometer.
- 55    **[0011]** Another object of the invention is to provide a system for detecting macromolecules, colloids and other particles of interest having diameters in the range of 3-1,000 nanometers, substantially without interference from residue artifacts.
- [0012]** A further object is to provide a source of uniform aerosols for testing particle detection and classification

devices within precisely defined ranges of particle diameters.

**[0013]** Yet another object is to provide a means for preparing uniform droplets sufficiently small to isolate single individual biological molecules, e.g. nucleic acids, proteins, and carbohydrates, for subsequent observation.

## 5 SUMMARY OF THE INVENTION

**[0014]** To achieve these and other objects, there is provided an apparatus for generating aerosols as claimed in claim 1.

**[0015]** Claim 1 provides an apparatus for generating aerosols, including:

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an electrospray means (20) having an electrospray inlet (22) and a discharge (74), for receiving a liquid sample at the electrospray inlet (22) and generating multiple substantially uniformly sized electrically charged droplets of the liquid sample at the discharge (74); a means (18) for supplying the liquid sample to the electrospray means (20); and an evaporation means (24) defining a droplet evaporation region (24) proximate the electrospray discharge (74) and extending downstream thereof, for reducing the size of the droplets by evaporation as the droplets progress downstream through the evaporation region (24), to form an aerosol of the sample; wherein the improvement comprises:

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a charge neutralizing means (88, 90, 92) disposed proximate the discharge (74) and along the evaporation region (24), for reducing the electrical charge of each droplet of the liquid sample as the droplet exits the electrospray means (22), and for continuing to reduce the electrical charge of each droplet as it progresses through the evaporation region (24) to prevent the droplets from disintegrating due to repulsive coulombic forces.

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**[0016]** The preferred neutralizing means is a source of ionizing radiation, for example radioactive polonium emitting alpha particles or a photon ionization source, or another source of ions, such as a corona discharge. The source of ions is positioned proximate the electrospray discharge, such that the droplets encounter the ions virtually immediately upon their formation. Additional sources of ions can be positioned further downstream along the evaporation region, so that the droplets are further neutralized as they proceed downstream.

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**[0017]** The evaporating means advantageously includes an enclosure defining an evaporation chamber having an entrance orifice just downstream of the electrospray discharge. The enclosure further can define an electrospray chamber adjacent and upstream of the evaporation chamber, with the electrospray discharge within the electrospray chamber. An electrically conductive plate or wall separates the evaporation chamber from the electrospray chamber and is electrically biased to attract the newly formed charged droplets toward the evaporation chamber. The entrance orifice, disposed in the wall, admits the droplets into the evaporation chamber.

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**[0018]** Preferably a gas is supplied to the electrospray chamber, and flows in a sheath or stream through the entrance orifice into the evaporation chamber, to carry the charged droplets into the evaporation chamber. A flow guide plate inside the electrospray chamber tends to diminish any turbulence in the gas flow, whereby newly formed droplets are carried smoothly and efficiently from the electrospray discharge into the evaporation chamber.

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**[0019]** The nebulizer is further enhanced by the addition of a vapor to the gas sheath, e.g. by adding the vapor to the gas supplied to the electrospray chamber. The vapor tends to retard evaporation of the droplets, further reducing the chance for droplet disintegration. The vapor can be water vapor, or more preferably, vapor of the solvent in the liquid sample. To further reduce evaporation rates, the air or other gas can be supplied to the evaporation chamber at a moderate temperature, i.e. with no preheating.

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**[0020]** Thus, electrostatically generated droplets of a liquid sample are uniform in size (i.e. monodisperse), not only as they are formed at the electrospray discharge, but also as they progress through the evaporation region to the nebulizer exit. The droplets proceed downstream across the evaporation region while subject to uniform conditions that substantially prevent their disintegration under Coulombic forces. Rayleigh disintegration is prevented, first by controlling the level of electrical charge in the droplets, more particularly in subjecting the droplets to charge-neutralizing radiation substantially immediately upon their formation and continuously as they progress along the evaporation region. The droplet carrying gas sheath provides further control, in more rapidly transferring droplets downstream to neutralizing radiation, effectively diminishing the rate of evaporation per unit distance of downstream travel. A further control is the amount of vapor in the gas stream, which of course further reduces droplet evaporation.

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**[0021]** The control of conditions in the nebulizer, whereby droplet disintegration is prevented, has yielded a surprising degree of size uniformity among droplets and other aerosols discharged by the nebulizer. This feature substantially enhances the utility and effectiveness of the nebulizer, particularly in combination with known devices for detecting and characterizing extremely small particles. For example, the nebulizer of the present invention can provide its output to a condensation particle counter (such as described in U.S. Patent No. 4,790,650) to monitor residue, measure concentrations of compounds and detect compounds in the threshold size range of the condensation particle counter (i.e. 3-1,000 nm diameter). The improved nebulizer can be used as a source of particles of a narrow, precisely controlled

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size range, to test a filter or characterize a particle measuring instrument. Further, the nebulizer can be used to deposit small and uniform droplets, to isolate single molecules (e.g. viruses, nucleic acids, proteins and carbohydrates) for analysis by techniques such as atomic force microscopy or electron microscopy.

[0022] Generally, the ability to control the nebulizer and avoid Coulomb disintegration, enables electrostatic generation of primary droplets smaller in size than previously believed feasible. More particularly, primary droplets are formed with diameters in the range of from about 140 to 860 nanometers in diameter, for residue particle diameters of substantially less than 10 nanometers, assuming a particle diameter of about 1 percent of the primary droplet diameter. Accordingly, macromolecules, colloids and other particles of interest with diameters in the range of 10 nanometers can be detected and characterized successfully using presently available analytical apparatus, such as the abovementioned condensation particle counter.

#### IN THE DRAWINGS

[0023] For a further appreciation of the above and other features and advantages, reference is made to the following detailed description and to the drawings, in which:

Figure 1 is a schematic view of a system for detecting and characterizing small particles in accordance with the present invention;

Figure 2 is a forward elevational view of an electrospray nebulizer employed in the system of Figure 1;

Figure 3 is a sectional view taken along the line 3-3 in Figure 2;

Figure 4 is an enlarged view of a portion of Figure 3;

Figure 5 is a sectional view taken along the line 5-5 in Figure 4;

Figure 6 is a schematic view of an alternative electrospray nebulizer;

Figure 7 is a schematic view of a particle separation and detection system according to another embodiment of the invention;

Figure 8 is a schematic view of a spectrochemical particle analyzing system according to a further embodiment of the invention; and

Figure 9 is a schematic view of biomedical particle analysis system according to yet another embodiment of the invention.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0024] Turning now to the drawings, there is shown in Figure 1 a system for detecting and characterizing particles in the range of from 3 to 1,000 nanometers in diameter. Initially, the particles of interest are part of a liquid sample or solution held in a container 16. A syringe pump 18, loaded with the liquid from the container, supplies the liquid to an electrospray nebulizer 20 at a steady, controlled rate, e.g. about 0.6 microliters per minute. The liquid of the sample can be water, with a volatile additive, e.g. either nitric acid or hydrochloric acid, added in a predetermined amount to control the electrical conductivity of the solution. Typically, the pH of the liquid sample is between four and five. Other additives are suitable for increasing conductivity, e.g. acetic acid and ammonium acetate. The primary reason for enhancing conductivity is to enable nebulizer 20 to produce smaller droplets, and thus smaller particles.

[0025] The nebulizer includes two chambers, an electrospray chamber 22 and an evaporation chamber 24. Syringe pump 18 supplies the liquid to the electrospray chamber. Another input to electrospray chamber 22 is a steady rate supply of a filtered gas, typically air. More particularly, air under pressure in a container 26 is provided through a valve 28 to a filter 30, and then via controlling orifice 32 to the nebulizer. Filter 30 is a high efficiency pleated glass filter available from TSI Incorporated of St. Paul, Minnesota and designated as Model 3074. Optionally, a heater (not illustrated) can be interposed between critical orifice 32 and nebulizer 20. Preferably, however, heated air (or another gas) is supplied to the nebulizer at evaporation chamber 24. As illustrated, air from a supply 34 is directed through a valve 36, a filter 38 and a controlling orifice 40 to a heater 42. Air from the heater enters the evaporation chamber, to maintain the temperature within chamber 24 at 32 degrees C. or more, to promote evaporation of droplets of the liquid sample.

[0026] A high voltage source 44 is electrically connected to a capillary needle 46 of the nebulizer, while portions of the nebulizer electrically isolated from the needle are connected to ground. Under certain circumstances it is preferable to ground the needle and bias such electrically isolated portions. In any event, the key is to create a high potential difference between the needle and the isolated portions.

[0027] The output of electrospray nebulizer 20 is provided to a differential mobility particle sizer (DMPS) 48, which consists of an electrostatic classifier 50 and a condensation particle counter (CPC) 52. An appropriate DMPS is available from TSI Incorporated as TSI Model 390074 including a TSI Model 3071 electrostatic classifier and a TSI Model 3025 condensation particle counter (sometimes known as a condensation nucleus counter).

[0028] The output of electrospray nebulizer 20 is an aerosol, and can include droplets (substantially reduced in size

but not yet fully evaporated), non-volatile residue from droplets that contained dissolved impurities, and isolated particles under study (e.g. macromolecules or colloids) together with non-volatile residue. The particle concentration in the liquid sample is sufficiently low, and the size of generated droplets is kept sufficiently small, thus substantially reducing the probability of generating doublets or other clusters of two or more molecules or colloids within a single droplet. For further information on this principle, reference is made to the aforementioned US-A-5 076 094.

**[0029]** The electrospray nebulizer output is provided to classifier 50, which operates based on the monotonic relationship between electrical mobility and size, of singly charged particles. Particles received in classifier 50 are introduced into a bipolar charger where they collide with bipolar ions, reaching an equilibrium state of known proportions of neutral particles, singly charged particles, and particles having multiple charges. Then particles are directed to a differential mobility analyzer having two concentric metal cylinders. The particles and air flow downwardly from the top of a gap between the cylinders, with a D.C. voltage applied to the inner cylinder while the outer cylinder is grounded. Particles of the appropriate polarity are attracted to the inner cylinder. Particles of a predetermined size reach the region of a narrow opening, where they are swept through by an air stream. Smaller particles adhere to the inner cylinder above the opening, while larger particles continue to descend below the opening.

**[0030]** Particles leaving electrostatic classifier 50 are detected and counted in condensation particle counter 52. In the condensation particle counter, the particles proceed through a region saturated with a vapor, e.g. n-butyl alcohol. Then, the particle stream is cooled sufficiently to supersaturate the vapor, whereupon the vapor condenses onto the particles, forming aerosol droplets much larger in diameter than the particles entering the CPC. Downstream of the condenser, the aerosol droplets are detected by an optical detector including a laser and associated optics. For further information about the CPC, reference is made to U.S. Patent No. 4,790,650 (Keady), assigned to the assignee of this application.

**[0031]** The output of the CPC is an electrical signal responsive to particles that pass through a viewing volume defined by the laser and optics. The signal is provided to a microcomputer 54, which analyzes the data and controls the classifier and the CPC. A suitable microcomputer is available from International Business Machines Corporation, as the IBM XT Model 286 personal computer. A salient feature of the present invention is the manner in which electrospray nebulizer 20 enhances the performance of DMPS 48, in particular by providing an aerosol composed of uniformly sized droplets or particles. The high degree of uniformity primarily is the result of the nebulizer structure as illustrated in Figures 2-5, although stabilized inputs to the nebulizer can enhance uniformity.

**[0032]** Various sections of the nebulizer are secured to one another to provide a fluid-tight enclosure. These sections include an electrospray cylinder 56, an evaporation cylinder 58, a capillary mounting end section 60, and an exit end section 62 opposite the capillary mounting section. All of the sections preferably are constructed of brass, stainless steel or other metal, and are provided with rectangular grooves, e.g. as indicated at 64, to accommodate sealing rings. A circular plate 66, also of brass or stainless steel, is mounted between the electrospray and evaporation cylinders to provide an electrically conductive wall between electrospray chamber 22 and evaporation chamber 24. An orifice 68 having a diameter of approximately 4.6 mm (0.18 inches) is located at the center of plate 66. An opening 69 through evaporation cylinder 58 admits heated and filtered air to the evaporation chamber. Further openings can be provided, if desired.

**[0033]** End section 60, when secured to electrospray cylinder 56 by screws, supports capillary needle 46 in a concentric alignment with the electrospray chamber. More particularly, the capillary needle is mounted within an elongate cylindrical metal casing 70, surrounded by an insulative jacket 72 constructed of a material selected for toughness, e.g. Delrin brand acetal (a plastic) available from duPont. The capillary needle, casing and jacket are housed within end section 60, with the jacket electrically isolating the capillary needle from the aluminum enclosure. Capillary needle 46 is elongate and suited for forming small droplets, with an outside diameter of about 0.5 mm (0.02 inches) and an interior (lumen) diameter of about 50 micrometers. A discharge 74 of the needle is positioned approximately 5.6 mm (0.22 inches) upstream of plate 66, concentric with orifice 68.

**[0034]** End section 60 has three segments, including an end cap 76, a narrow shank 78, and a flow guide plate 80. The shank is aligned with an opening 82 through electrospray cylinder 56, through which the filtered air enters the electrospray chamber. As seen in Figure 5, multiple 1 mm (0.04 inch) diameter guide apertures 84 are formed through guide plate 80 in a pattern of circles concentric on capillary needle 46. Guide apertures 84 cooperate to channel the flow of air, to form an air "sheath" surrounding capillary needle 46 and flowing along the needle and into evaporation chamber 24 through orifice 68. Guide apertures 84 substantially reduce turbulence in the gas flow, permitting an increased flow velocity whereby the gas sheath more rapidly transfers charged droplets into the evaporation chamber.

**[0035]** Electrospray chamber 22 includes a radially enlarged region 86 near plate 66. Along this region, a strip 88 of radioactive polonium is mounted to cylinder 56, and provides a source of ionizing radiation within the electrospray chamber, particularly along the region between discharge 74 and orifice 68. Similar strips are mounted to the evaporation cylinder as indicated at 90 and 92, and provide ionizing radiation throughout the evaporation chamber. The ions encounter the sample droplets produced at discharge 74, and reduce their electrical charge, tending to neutralize the droplets. Due to the presence of strip 88, droplets encounter the ions virtually immediately upon their formation, which

minimizes the potential for droplet disintegration due to Coulombic forces.

**[0036]** Strips 90 and 92 provide ionizing radiation in the evaporation chamber, to prevent Coulomb disintegration as droplets of the sample proceed through the evaporation chamber and for the further purpose of preventing the droplets from clinging to the evaporation cylinder.

**[0037]** It has been found that mounting radiation sources to the evaporation cylinder alone provides sufficient neutralization, if a source of the radiation is positioned sufficiently upstream to provide substantial radiation at orifice 68. Also, it is to be recognized that ion sources other than polonium strips can be employed, for example corona discharge sources 94, 96 and 98 as indicated in a nebulizer 100 (Figure 6), a photon ionization source, or any radioactive material emitting alpha particles or beta particles.

**[0038]** When electrospray nebulizer 20 is to be used, voltage source 44 is connected to bias capillary needle 46 to a predetermined voltage in the range of from about 1.5-10 kilovolts, or more preferably 2-3 kilovolts. Syringe pump 18 supplies that sample solution at a steady rate of about 0.6 microliters per minute. Filtered air is supplied to the electrospray chamber 22 at the rate of about 2.5 liters per minute. The applied voltage creates an electrical field between capillary needle 46 and the surrounding grounded structure, in particular between discharge 74 and plate 66. As the sample solution emerges at the discharge, the surface of the liquid is charged, with Coulombic forces eventually overcoming cohesive forces such as surface tension, thereby causing a primary droplet to break away from the liquid remaining in the needle. Multiple repetitions of this phenomenon create a mist of solution droplets, substantially uniform in their diameter. The primary droplets are attracted toward plate 66 due to their charge, and carried through orifice 68 in the air sheath.

**[0039]** Almost immediately as they emerge from capillary needle 46, the solution droplets begin to shrink due to evaporation of the volatile solvent of the sample solution. If each of the droplets were to retain its electrical charge, the surface charge density would of course increase as the droplet size is reduced. Eventually, Coulombic forces would overcome cohesive forces such as surface tension, causing each droplet to disintegrate into a plurality of smaller droplets. Coulomb disintegration, occurring generally throughout the aerosol, would destroy the size uniformity of the droplets.

**[0040]** The polonium strips and guide plate 80 are features utilized to control conditions within the nebulizer, thus to prevent Coulomb disintegration. More particularly, ions produced by the alpha particle radiation reduce the charge of each droplet as it is reduced in size, retarding what otherwise would be a rapid increase in charge density at the surface of each droplet. The guide plate channels and controls the air flow, permitting a higher velocity air sheath. Consequently, droplets are transmitted more rapidly to the evaporation region, effectively reducing the rate of evaporation per unit length of aerosol travel. As the consequence of these features, the charged droplets remain uniform in size, not only within electrospray chamber 22 but throughout their travel across evaporation chamber 24, so that a monodisperse aerosol is presented to the differential mobility particle sizer or other instrument. In fact, it is the particle size uniformity of the nebulizer output that allows use of the DMPS in lieu of the chromatography system and CPC described in US-A-5 076 097, for a faster, less cumbersome system that affords improved resolution.

**[0041]** Figure 7 illustrates an electrospray nebulizer 102 in a system involving particle separation based on liquid chromatography. The output of a liquid chromatography system 104, i.e. a separated liquid sample solution, is provided at a controlled rate to electrospray nebulizer 102 which is substantially identical to nebulizer 20 and has an electrospray chamber 106 and an evaporation chamber 108. An air supply 110, a valve 112, a filter 114 and a controlling orifice 116 are employed in providing filtered air to the electrospray chamber. In accordance with a further aspect of the present invention, air from the critical orifice travels through a chamber 118 on its way to the nebulizer. A polonium strip 120, or other suitable source of ionizing radiation mounted within chamber 118, produces bipolar ions within the chamber. These ions are swept along in the air stream and sheath surrounding a capillary needle 122 of the nebulizer, thus to prevent fragmentation of the droplets at the earliest possible stage. This prevents the loss of droplets to the walls of electrospray chamber 106. Further polonium strips 124 and 126 are positioned within evaporation chamber 108. In view of polonium strip 120, a similar strip within the electrospray chamber is not necessary, although a strip could be utilized in chamber 106, if desired. The nebulizer output is provided to a diffusion screen 128, then to a condensation particle counter 130.

**[0042]** Figure 8 illustrates a further embodiment system in which particles are subject to spectrochemical analysis. More particularly, a syringe pump 132 meters a liquid sample solution, loaded from a container 134, into an electrospray chamber 136 of an electrospray nebulizer 138. As before, air from a supply 140 is directed through a valve 142 to a filter 144. From filter 144, however, the air is provided to a closed container 146 containing a liquid 148. Air exiting the container thus includes a vapor of the liquid. The vapor-containing air proceeds through a controlling orifice 150, and into electrospray chamber 136. Ionization radiation sources 152, 154 and 156 in the nebulizer prevent Coulomb fragmentation, in the manner previously described.

**[0043]** The output of electrospray nebulizer 138 is provided to a spectrochemical configuration 158, which can include instruments for known spectrochemical techniques such as inductive coupled plasma, atomic absorption spectrometry, and atomic emission spectrometry.

[0044] Figure 9 illustrates a system for studying individual biological molecules, e.g. nucleic acids, proteins, carbohydrates and viruses. The molecules of interest are dispersed in a liquid medium such as water, alcohol or a buffer. The solution, consisting essentially of the medium and molecule dispersion from a container 160, is supplied at a steady rate to a chamber 162 of an electrospray nebulizer 164, using a syringe pump 166. For example, molecules of the enzyme phosphorylase kinase can be prepared in a 0.1 millimolar tris buffer having a specific conductivity of 64 micromhos/cm and a pH of 7 for this purpose. Filtered air also is supplied to the electrospray chamber as indicated generally at 168, and a supply of heated and filtered air is provided to the nebulizer, as seen at 170. A high voltage source 174 biases a capillary needle 176 to a predetermined level, while surrounding structure is grounded.

[0045] Electrospray nebulizer 164 differs from previously described nebulizers in that it defines a single chamber rather than separate electrospray and evaporation chambers. A flow guide plate 178 is mounted upstream of the needle discharge, whereby the filtered air forms a sheath surrounding the needle. If desired, the air can be preheated, and also humidified with water vapor or a vapor of the liquid medium. A relatively large orifice 180 is formed in a downstream end wall 182 of the nebulizer.

[0046] A graphite plate 184 is mounted on a metal support rod 186, and positioned immediately downstream of the exit orifice. The plate and support rod are grounded, whereby sample solution droplets are attracted to the plate, as well as being carried toward the plate by the air sheath. A motor 188 rotates plate 184 through rod 186, about an axis through the center of the rod, which tends to even the distribution of collected droplets over the surface of the plate.

[0047] The different structure of nebulizer 164 is suited to its purpose. In particular, droplets intentionally are not evaporated to completely dry the aerosol. Rather, sufficient medium is retained, at least initially, to surround and support the molecule under study.

[0048] Following deposition, plate 184 is removed from rod 186. Individual molecules are analyzed, e.g. using atomic force microscopy, scanning tunneling microscopy, or transmission electron microscopy.

[0049] A feature of the present invention is that the electrospray nebulizer provides a heretofore unachieved degree of control over the nebulizer output, in terms of aerosol size as well as uniformity. Factors such as conductivity of the liquid solution sample, flow rate at which the sample is supplied to the nebulizer, and the voltage applied to form the electrical field, control the diameter of primary droplets. More particularly, droplet size can be reduced by increasing solution conductivity, increasing the needle/plate voltage, and reducing the liquid flow rate. The following table of experimental results illustrates the effect of changes in flow rate and conductivity on droplet size:

FLOW RATE MICROLITERS PER MINUTE	SPECIFIC CONDUCTIVITY MICROMHOS PER CM	DROPLET SIZE MICROMETERS
0.76	830	0.86
0.5	813	0.8
0.2	1,190	0.53
0.075	2,600	0.256

[0050] In practice, the conductivity required for a given droplet size and flow rate can vary widely depending on the solvents involved, e.g. over a range of from about 10-100,000 micromhos per centimeter.

[0051] Given the uniform distribution of residue throughout a liquid sample, the size of dried residue particles exhibits similar uniformity and is subject to the same control. Consequently, a nebulizer of the type disclosed can be used as a source of uniformly sized particles, over different ranges and levels of sizes, to test a filter, and to characterize a particle analyzing instrument such as a condensation particle counter.

[0052] Thus, an electrospray nebulizer is provided for producing primary droplets of uniform size and substantially below one micron in diameter. Primary droplets are subjected to neutralizing radiation shortly after their formation, to prevent Rayleigh disintegration and thereby maintain a high degree of size uniformity despite reduction in droplet size due to solvent evaporation. The nebulizer thus produces an aerosol of smaller, more uniformly sized particles. The performance of particle analyzing instruments receiving the nebulizer output is substantially enhanced, and the nebulizer can provide a source of uniformly sized particles for testing of such instruments.

## Claims

1. An apparatus for generating aerosols, including:

an electrospray means (20) having an electrospray inlet (22) and a discharge (74), for receiving a liquid sample at the electrospray inlet (22) and generating multiple substantially uniformly sized electrically charged droplets

of the liquid sample at the discharge (74); a means (18) for supplying the liquid sample to the electrospray means (20); and an evaporation means (24) defining a droplet evaporation region (24) proximate the electrospray discharge (74) and extending downstream thereof, for reducing the size of the droplets by evaporation as the droplets progress downstream through the evaporation region (24), to form an aerosol of the sample; wherein the improvement comprises:

a charge neutralizing means (88, 90, 92) disposed proximate the discharge (74) and along the evaporation region (24), for reducing the electrical charge of each droplet of the liquid sample as the droplet exits the electrospray means (20), and for continuing to reduce the electrical charge of each droplet as it progresses through the evaporation region (24) to prevent the droplets from disintegrating due to repulsive coulombic forces.

2. The apparatus of Claim 1 wherein:

the evaporation means (24) includes an enclosure (58) defining an evaporation chamber (24) having an entrance orifice (68) and an exit (62), and providing said evaporation region.

3. The apparatus of Claim 2 wherein:

the enclosure (56, 58) further defines an electrospray chamber (22) adjacent the evaporation chamber (24), said discharge (74) being within the electrospray chamber (22); and

wherein the enclosure (56, 58) further includes an electrically conductive wall (66) separating the evaporation chamber (24) from the electrospray chamber (22) and electrically biased to attract the electrically charged droplets toward the evaporation chamber (24), and the entrance orifice (68) is disposed in the electrically conductive wall (66).

4. The apparatus of Claim 2 or 3 wherein:

the neutralizing means (88, 90, 92) includes a first ion producing means (90) in the evaporation chamber (24) near the entrance orifice (68).

5. The apparatus of Claim 4 wherein:

the neutralizing means (88, 90, 92) further includes a second ion producing means (88), located in the electrospray chamber (22).

6. The apparatus of Claim 4 wherein:

the ion producing means (88, 90, 92) comprises at least one of the following: a radioactive material emitting alpha particles, a radioactive material emitting beta particles, a corona discharge source, and a photon ionization source.

7. The apparatus of any one of Claims 3 to 6 further including:

a means (26, 28, 30, 32) for supplying a gas to the electrospray chamber (22) and flowing in a stream from the electrospray chamber (22) into the evaporation chamber (24), thereby tending to carry the electrically charged droplets into the evaporation chamber (24).

8. The apparatus of Claim 7 further including:

a means (84) in the electrospray chamber (22) for substantially reducing the turbulence of the gas stream.

9. The apparatus of any preceding claim further including:

a means (26, 28, 30, 32, 80) for retarding the rate of evaporation of the liquid.

10. The apparatus of Claim 9 wherein:

said means for retarding the rate of evaporation include means (140, 142, 144, 146, 148, 150) for introducing vapor of the liquid into the evaporation region (24).

11. The apparatus of any preceding claim further including:

a means (26, 28, 30, 32, 80) for providing a gas stream along the electrospray means (20) for carrying the electrically charged droplets downstream through the evaporation region (24).

12. The apparatus of any preceding claim wherein:

the electrospray means (20) includes an elongate capillary needle (46) defining an elongate lumen having



an inlet port and an exit port (74) on opposite ends of the capillary needle (46), said exit port (74) providing said discharge.

13. The apparatus of any preceding claim further including:  
5 an analyzing means (48, 130, 158) disposed downstream of the evaporation region (24) to receive the aerosol.
14. The apparatus of Claim 13 wherein:  
10 the analyzing means (48, 130, 158) includes a particle separation means (50) and a particle counting means (52) disposed downstream of the particle separation means (50).
15. The apparatus of Claim 14 wherein:  
the particle separation means (50) separates particles of the aerosol based upon electrical mobility of the individual particles.  
15
16. The apparatus of any one of Claims 1 to 12 further including:  
a particle counting means (52) disposed downstream of the evaporation region (24) to receive the aerosol.
17. The apparatus of any one of Claims 14 to 16 wherein:  
20 the particle counting means (52) is a condensation particle counter.
18. The apparatus of any one of Claims 1 to 12 further including:  
an aerosol collection means (184) proximate to and downstream of the evaporation region (24).
- 25 19. The apparatus of Claim 14 or Claim 15 wherein:  
the aerosol collection means comprises an electrically charged plate (184).
20. The apparatus of Claim 14 or Claim 15 wherein:  
30 the separation means comprises an electrostatic classifier (50).
21. A process for forming multiple submicron droplets generally uniform in size, including the steps of:  
  
providing a liquid sample at a steady supply rate to an electrospray device (20), and generating multiple,  
35 substantially uniformly sized, electrically charged droplets of the liquid sample at a discharge (74) of the electrospray device (20);  
transporting the electrically charged droplets downstream of the discharge (74) through an evaporation region (24), to controllably reduce the size of the droplets by evaporation as the droplets progress through the evaporation region (24);  
40 while so transporting the droplets, reducing the electrical charge of each droplet as it emerges from the discharge; and thereafter continually reducing the electrical charge of each droplet as it is so transported, to prevent the droplet from disintegrating due to repulsive Coulombic forces.
22. The process of Claim 21 wherein:  
45 the liquid sample includes an electrically conductive liquid and a substantially non-volatile material dispersed substantially uniformly throughout the liquid, whereby the electrically charged droplets include the liquid and non-volatile residue consisting essentially of the material.
23. The process of Claim 22 wherein:  
50 the step of controllably reducing the size of the droplets includes evaporating substantially all of the electrically conductive liquid to form particles of the non-volatile residue.
24. The process of Claim 22 or 23 further including the step of:  
retarding the rate of evaporation of the electrically conductive liquid as the droplets progress through the evaporation region (24).  
55
25. The process of Claim 24 wherein:  
the electrically conductive liquid is a solvent, and the step of retarding the rate of evaporation includes supplying a gas stream to the evaporation region (24) with the gas stream including a vapor of the solvent.

26. The process of any one of Claims 21 to 25 including the further step of:  
controlling the specific conductivity of the liquid sample, whereby the conductivity is within the range of from  
about 10 micromhos/cm to about 100,000 micromhos/cm.

5 27. The process of Claim 26, wherein the electrically conductive liquid includes water and a volatile, ionizable solute.

# Patentansprüche

10 1. Gerät zum Erzeugen von Aerosolen mit:

einer Elektrosprüheinrichtung (20) mit einem Elektrosprüheinlaß (22) und einem Auslaß (74) zum Empfangen  
einer Flüssigkeitsprobe am Elektrosprüheinlaß (22) und Erzeugen mehrerer, im wesentlichen einheitlich gro-  
15 ßer, elektrisch geladener Tröpfchen der Flüssigkeitsprobe am Auslaß (74); einer Einrichtung (18) zum Zufüh-  
ren der Flüssigkeitsprobe zur Elektrosprüheinrichtung (20); und einer einen Tröpfchenverdampfungsbereich  
(24) nahe dem Elektrosprühauslaß (74) definierenden und Stromabwärts davon verlaufenden Verdampfungsbereichs-  
einrichtung (24) zum Reduzieren der Größe der Tröpfchen durch Verdampfung, während sich die Tröpfchen  
durch den Verdampfungsbereich (24) stromabwärts bewegen, um ein Aerosol der Probe zu bilden; worin die  
Verbesserung aufweist:

20 eine nahe dem Auslaß (74) und entlang dem Verdampfungsbereich (24) angeordnete Ladungsneutralisier-  
einrichtung (88, 90, 92) zum Reduzieren der elektrischen Ladung jedes Tröpfchens der Flüssigkeitsprobe,  
während das Tröpfchen die Elektrosprüheinrichtung (20) verläßt, und zum Fortsetzen des Reduzierens der  
elektrischen Ladung jedes Tröpfchens, während es sich durch den Verdampfungsbereich (24) bewegt, um zu  
verhindern, daß die Tröpfchen aufgrund abstoßender Coulombkräfte zerfallen.

25

2. Gerät nach Anspruch 1, worin:

die Verdampfungseinrichtung (24) ein Gehäuse (58) enthält, das eine Verdampfungskammer (24) mit einer  
Eingangsöffnung (68) und einem Ausgang (62) definiert und den Verdampfungsbereich liefert.

30 3. Gerät nach Anspruch 2, worin:

das Gehäuse (56, 58) ferner eine der Verdampfungskammer (24) benachbarte Elektrosprühkammer (22) de-  
finiert, wobei der Auslaß (74) innerhalb der Elektrosprühkammer (22) liegt; und  
worin das Gehäuse (56, 58) ferner eine elektrisch leitfähige Wand (66) enthält, die die Verdampfungskammer  
35 (24) von der Elektrosprühkammer (22) trennt und elektrisch vorgespannt ist, um die elektrisch geladenen  
Tröpfchen zur Verdampfungskammer (24) hin anzuziehen, und die Eingangsöffnung (68) in der elektrisch  
leitfähigen Wand (66) angeordnet ist.

40 4. Gerät nach Anspruch 2 oder 3, worin:

die Neutralisiereinrichtung (88, 90, 92) eine erste Ionenerzeugungseinrichtung (90) in der Verdampfungsk-  
ammer (24) nahe der Eingangsöffnung (68) enthält.

5. Gerät nach Anspruch 4, worin:

45 die Neutralisiereinrichtung (88, 90, 92) ferner eine zweite Ionenerzeugungseinrichtung (88) enthält, die in  
der Elektrosprühkammer (22) angeordnet ist.

6. Gerät nach Anspruch 4, worin:

50 die Ionenerzeugungseinrichtung (88, 90, 92) zumindest eine der folgenden aufweist: ein Alphateilchen emit-  
tierendes radioaktives Material, ein Betateilchen emittierendes radioaktives Material, eine Koronaentladungsquelle  
und eine Photonenionisationsquelle.

7. Gerät nach einem der Ansprüche 3 bis 6, ferner mit:

65 einer Einrichtung (26, 28, 30, 32) zum Zuführen eines Gases zur Elektrosprühkammer (22) und Einströmen  
eines Stroms von der Elektrosprühkammer (22) in die Verdampfungskammer (24), um dadurch dazu beizutragen,  
daß die elektrisch geladenen Tröpfchen in die Verdampfungskammer (24) befördert werden.

8. Gerät nach Anspruch 7, ferner mit:

einer Einrichtung (84) in der Elektrosprühkammer (22), um die Turbulenz des Gasstroms im wesentlichen

zu reduzieren.

9. Gerät nach einem der vorhergehenden Ansprüche, ferner mit:  
einer Einrichtung (26, 28, 30, 32, 80) zum verzögern der Verdampfungsrate der Flüssigkeit.
10. Gerät nach Anspruch 9, worin:  
die Einrichtung zum Verzögern der Verdampfungsrate Mittel (140, 142, 144, 146, 148, 150) zum Einführen von Dampf der Flüssigkeit in den Verdampfungsbereich (24) enthält.
11. Gerät nach einem der vorhergehenden Ansprüche, ferner mit:  
einer Einrichtung (26, 28, 30, 32, 80) zum Vorsehen eines Gasstroms entlang der Elektroprüheinrichtung (20) zum Befördern der elektrisch geladenen Tröpfchen stromabwärts durch den Verdampfungsbereich (24).
12. Gerät nach einem der vorhergehenden Ansprüche, worin:  
die Elektroprüheinrichtung (20) eine langgestreckte Kapillarnadel (46) enthält, die ein langgestrecktes Lumen mit einer Einlaßöffnung und einer Austrittsöffnung (74) an gegenüberliegenden Enden der Kapillarnadel (46) definiert, wobei die Austrittsöffnung (74) den Auslaß liefert.
13. Gerät nach einem der vorhergehenden Ansprüche, ferner mit:  
einer Analysiereinrichtung (48, 130, 158), die stromabwärts des Verdampfungsbereichs (24) angeordnet ist, um das Aerosol zu empfangen.
14. Gerät nach Anspruch 13, worin:  
die Analysiereinrichtung (48, 130, 158) eine Teilchentrenneinrichtung (50) und eine Teilchenzähleinrichtung (52) enthält, die stromabwärts der Teilchentrenneinrichtung (50) angeordnet ist.
15. Gerät nach Anspruch 14, worin:  
die Teilchentrenneinrichtung (50) Teilchen des Aerosols auf der Basis elektrischer Beweglichkeit der einzelnen Teilchen trennt.
16. Gerät nach einem der Ansprüche 1 bis 12, ferner mit:  
einer Teilchenzähleinrichtung (52), die stromabwärts des Verdampfungsbereichs (24) angeordnet ist, um das Aerosol zu empfangen.
17. Gerät nach einem der Ansprüche 14 bis 16, worin:  
die Teilchenzähleinrichtung (52) ein Kondensationsteilchenzähler ist.
18. Gerät nach einem der Ansprüche 1 bis 12, ferner mit:  
einer Aerosolsammeleinrichtung (184), die nahe dem Verdampfungsbereich (24) und stromabwärts davon angeordnet ist.
19. Gerät nach Anspruch 14 oder Anspruch 15, worin:  
die Aerosolsammeleinrichtung eine elektrisch geladene Platte (184) aufweist.
20. Gerät nach Anspruch 14 oder Anspruch 15, worin:  
die Trenneinrichtung einen elektrostatischen Klassierer (50) aufweist.
21. Verfahren zum Bilden mehrerer Submikrometertröpfchen mit im allgemeinen einheitlicher Größe mit den Schritten:  
Liefern einer Flüssigkeitsprobe mit einer gleichbleibenden Zufuhr rate an eine Elektroprühvorrückung (20) und Erzeugen mehrerer, im wesentlichen einheitlich großer, elektrisch geladener Tröpfchen der Flüssigkeitsprobe an einem Auslaß (74) der Elektroprühvorrückung (20);  
Transportieren der elektrisch geladenen Tröpfchen stromabwärts des Auslasses (74) durch einen Verdampfungsbereich (24), um die Größe der Tröpfchen durch Verdampfung steuerbar zu reduzieren, während sich die Tröpfchen durch den Verdampfungsbereich (24) bewegen;  
während dieses Transportierens der Tröpfchen, Reduzieren der elektrischen Ladung jedes Tröpfchens, während es aus dem Auslaß austritt, und anschließendes kontinuierliches Reduzieren der elektrischen Ladung jedes Tröpfchens, während es so transportiert wird, um zu verhindern, daß das Tröpfchen aufgrund absto-

Bender Coulombkräfte zerfällt.

**22. Verfahren nach Anspruch 21, worin:**

5 die Flüssigkeitsprobe eine elektrisch leitfähige Flüssigkeit und ein im wesentlichen nicht flüchtiges Material enthält, das in der ganzen Flüssigkeit im wesentlichen gleichmäßig dispergiert ist, wodurch die elektrisch geladenen Tröpfchen die Flüssigkeit und einen nicht flüchtigen Rest enthalten, der im wesentlichen aus dem Material besteht.

**23. Verfahren nach Anspruch 22, worin:**

10 der Schritt des steuerbaren Reduzierens der Größe der Tröpfchen ein Verdampfen von im wesentlichen der gesamten elektrisch leitfähigen Flüssigkeit einschließt, um Teilchen aus dem nicht flüchtigen Rest zu bilden.

**24. Verfahren nach Anspruch 22 oder 23, ferner mit dem Schritt eines:**

15 Verzögerens der Verdampfungsrate der elektrisch leitfähigen Flüssigkeit, während die Tröpfchen sich durch den Verdampfungsbereich (24) bewegen.

**25. Verfahren nach Anspruch 24, worin:**

20 die elektrisch leitfähige Flüssigkeit ein Lösungsmittel ist und der Schritt des Verzögerens der Verdampfungsrate ein Zuführen eines Gasstroms zum Verdampfungsbereich (24) einschließt, wobei der Gasstrom Dampf des Lösungsmittels enthält.

**26. Verfahren nach einem der Ansprüche 21 bis 25, mit dem weiteren Schritt eines:**

25 Steuerns der spezifischen Leitfähigkeit der Flüssigkeitsprobe, wodurch die Leitfähigkeit innerhalb des Bereichs von etwa 10 Mikrosiemens/cm (engl. micromhos/cm) bis 100000 Mikrosiemens/cm liegt.

**27. Verfahren nach Anspruch 26, worin die elektrisch leitfähige Flüssigkeit Wasser und einen flüchtigen, ionisierbaren gelösten Stoff enthält.**

**30 Revendications**

**1. Appareil de production d'aérosols, comprenant :**

35 un moyen électro-atomiseur (20) muni d'une admission d'électro-atomisation (22) et d'une évacuation (74), pour recevoir un échantillon liquide à l'admission d'électro-atomisation (22) et pour engendrer, à l'évacuation (74), de multiples gouttelettes de l'échantillon liquide qui présentent une taille pour l'essentiel uniforme et sont chargées électriquement ; un moyen (18) pour délivrer l'échantillon liquide au moyen électro-atomiseur (20) ; et un moyen d'évaporation (24) définissant une zone (24) d'évaporation des gouttelettes, voisine de l'évacuation d'électro-atomisation (74) et s'étendant vers l'aval de cette dernière, afin de réduire la taille des goutte-  
40 lettes, par évaporation, au fur et à mesure que les gouttelettes progressent vers l'aval à travers la zone d'évaporation (24), en vue de former un aérosol de l'échantillon ; le perfectionnement comprenant : un moyen (88, 90, 92) de neutralisation de charge, disposé à proximité de l'évacuation (74) et le long de la zone d'évaporation (24), pour réduire la charge électrique de chaque gouttelette de l'échantillon liquide lorsque ladite gouttelette sort du moyen électro-atomiseur (20), et pour continuer de réduire la charge électrique de  
45 chaque gouttelette lorsqu'elle progresse à travers la zone d'évaporation (24), afin d'empêcher une désintégration des gouttelettes sous l'action de forces répulsives de Coulomb.

**2. Appareil selon la revendication 1, dans lequel :**

50 le moyen d'évaporation (24) comporte une enceinte (58) définissant une chambre d'évaporation (24) munie d'un orifice d'entrée (68) et d'une sortie (62), et matérialisant ladite zone d'évaporation.

**3. Appareil selon la revendication 2, dans lequel :**

55 l'enceinte (56, 58) définit, en outre, une chambre d'électro-atomisation (22) adjacente à la chambre d'évaporation (24), ladite évacuation (74) se trouvant à l'intérieur de la chambre d'électro-atomisation (22) ; et dans lequel l'enceinte (56, 58) présente, par ailleurs, une paroi (66) électriquement conductrice séparant la chambre d'évaporation (24) d'avec la chambre d'électro-atomisation (22), et polarisée électriquement pour attirer les gouttelettes, chargées électriquement, en direction de la chambre d'évaporation (24), et l'orifice

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d'entrée (68) est pratiqué dans la paroi (66) électriquement conductrice.

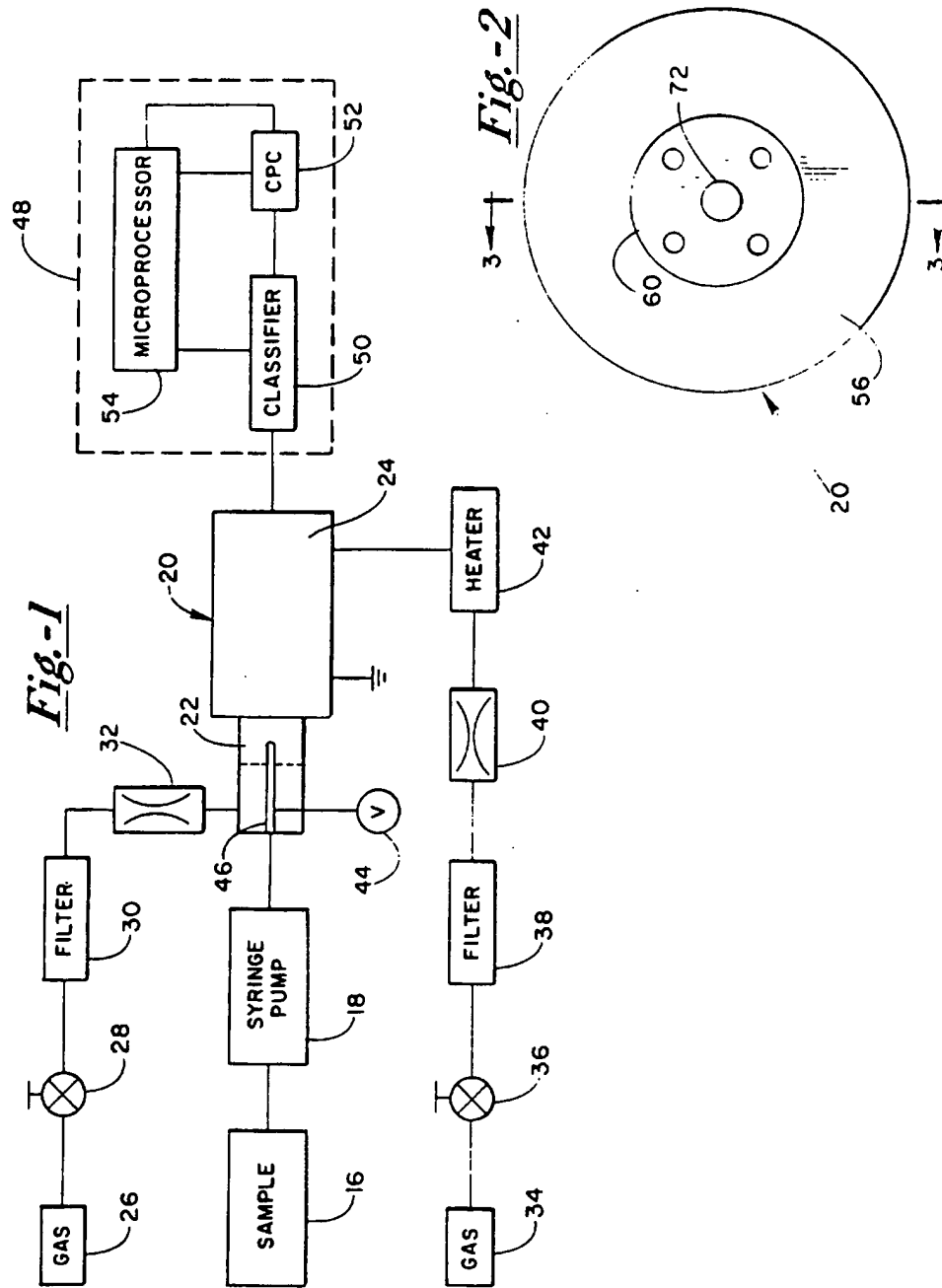
4. Appareil selon la revendication 2 ou 3, dans lequel :  
le moyen de neutralisation (88, 90, 92) présente un premier moyen (90) générateur d'ions, dans la chambre d'évaporation (24), à proximité de l'orifice d'entrée (68).
5. Appareil selon la revendication 4, dans lequel :  
le moyen de neutralisation (88, 90, 92) présente, en outre, un second moyen (88) générateur d'ions qui est logé dans la chambre d'électro-atomisation (22).
6. Appareil selon la revendication 4, dans lequel :  
le moyen (88, 90, 92) générateur d'ions comprend au moins l'un des éléments suivants : une matière radioactive émettant des particules alpha, une matière radioactive émettant des particules bêta, une source de décharge à effet corona, et une source d'ionisation photonique.
7. Appareil selon l'une quelconque des revendications 3 à 6, comprenant en outre :  
un moyen (26, 28, 30, 32) conçu pour délivrer un gaz à la chambre d'électro-atomisation (22), et s'étendant en succession continue depuis ladite chambre d'électro-atomisation (22) jusque dans la chambre d'évaporation (24), tendant ainsi à faire pénétrer, dans ladite chambre d'évaporation (24), les gouttelettes chargées électriquement.
8. Appareil selon la revendication 7, comprenant en outre :  
un moyen (84) situé dans la chambre d'électro-atomisation (22), pour réduire notablement la turbulence de l'écoulement gazeux.
9. Appareil selon une quelconque revendication précédente, comprenant en outre :  
un moyen (26, 28, 30, 32, 80) pour ralentir la vitesse d'évaporation du liquide.
10. Appareil selon la revendication 9, dans lequel :  
ledit moyen, destiné à ralentir la vitesse d'évaporation, comporte des moyens (140, 142, 144, 146, 148, 150) pour introduire de la vapeur du liquide dans la zone d'évaporation (24).
11. Appareil selon une quelconque revendication précédente, comprenant en outre :  
un moyen (26, 28, 30, 32, 80) pour engendrer un écoulement gazeux le long du moyen électro-atomiseur (20), afin d'acheminer vers l'aval, à travers la zone d'évaporation (24), les gouttelettes chargées électriquement.
12. Appareil selon une quelconque revendication précédente, dans lequel :  
le moyen électro-atomiseur (20) comporte une aiguille capillaire allongée (46), définissant une cavité longue pourvue d'un orifice d'admission et d'un orifice de sortie (74) à des extrémités opposées de l'aiguille capillaire (46), ledit orifice de sortie (74) matérialisant ladite évacuation.
13. Appareil selon une quelconque revendication précédente, comprenant en outre :  
un moyen analyseur (48, 130, 158) disposé en aval de la zone d'évaporation (24), pour recevoir l'aérosol.
14. Appareil selon la revendication 13, dans lequel :  
le moyen analyseur (48, 130, 158) comprend un moyen (50) de séparation de particules et un moyen (52) de comptage de particules, installé en aval dudit moyen (50) de séparation de particules.
15. Appareil selon la revendication 14, dans lequel :  
le moyen (50) de séparation de particules sépare des particules de l'aérosol sur la base d'une mobilité électrique des particules individuelles.
16. Appareil selon l'une quelconque des revendications 1 à 12, comprenant en outre :  
un moyen (52) de comptage de particules disposé en aval de la zone d'évaporation (24), pour recevoir l'aérosol.
17. Appareil selon l'une quelconque des revendications 14 à 16, dans lequel :  
le moyen (52) de comptage de particules est un compteur de particules à condensation.

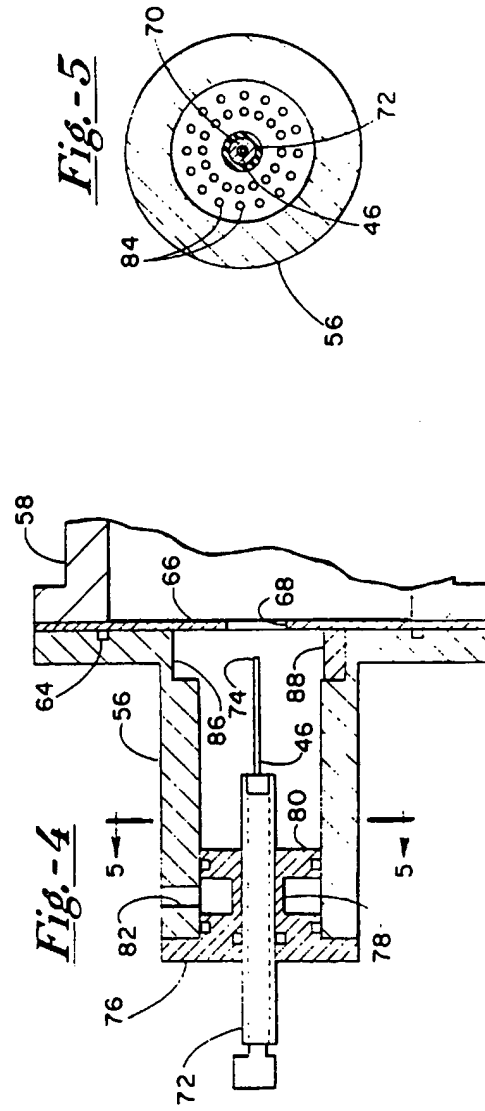
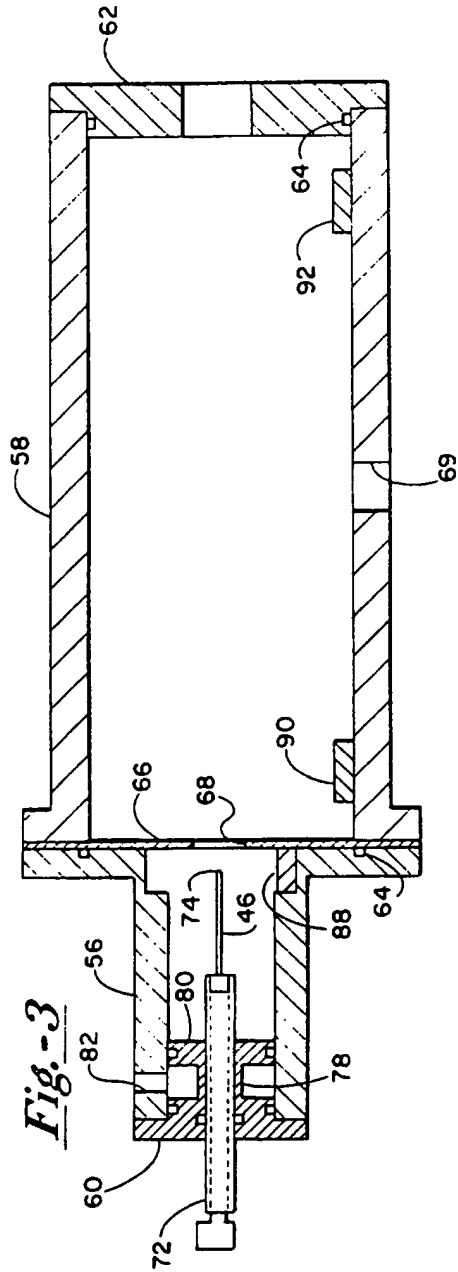
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18. Appareil selon l'une quelconque des revendications 1 à 12, comprenant en outre :  
un moyen (184) collecteur d'aérosol, situé à proximité de la zone d'évaporation (24) et en aval de cette dernière.
- 5 19. Appareil selon la revendication 14 ou la revendication 15, dans lequel :  
le moyen collecteur d'aérosol comprend une platine (184) chargée électriquement.
20. Appareil selon la revendication 14 ou la revendication 15, dans lequel :  
le moyen de séparation comprend un classificateur électrostatique (50).
- 10 21. Procédé de formation de multiples gouttelettes d'une taille généralement uniforme, inférieure au micromètre, comprenant les étapes consistant :
- 15 à délivrer un échantillon liquide à un dispositif électro-atomiseur (20), selon une vitesse d'alimentation constante, et à engendrer, à une évacuation (74) dudit dispositif électro-atomiseur (20), de multiples gouttelettes de l'échantillon liquide qui présentent une taille pour l'essentiel uniforme et sont chargées électriquement ;  
à transporter les gouttelettes chargées électriquement vers l'aval de l'évacuation (74), à travers une zone d'évaporation (24), pour réduire la taille des gouttelettes de manière commandée, par évaporation, au fur et  
20 à mesure que les gouttelettes progressent à travers la zone d'évaporation (24) ;  
tout en transportant ainsi les gouttelettes, à réduire la charge électrique de chaque gouttelette lorsqu'elle sort de l'évacuation ; et à réduire ensuite continuellement la charge électrique de chaque gouttelette, lorsqu'elle est ainsi transportée, afin d'empêcher une désintégration de la gouttelette sous l'action de forces répulsives de Coulomb.
- 25 22. Procédé selon la revendication 21, dans lequel :  
l'échantillon liquide comprend un liquide électriquement conducteur et une matière pour l'essentiel non volatile dispersée pour l'essentiel uniformément dans le liquide, de sorte que les gouttelettes, chargées électriquement, contiennent le liquide et un résidu non volatil essentiellement constitué de la matière.
- 30 23. Procédé selon la revendication 22, dans lequel :  
l'étape de réduction de la taille des gouttelettes, de manière commandée, consiste à évaporer en substance la totalité du liquide électriquement conducteur, pour former des particules du résidu non volatil.
24. Procédé selon la revendication 22 ou 23, comprenant en outre l'étape consistant à :  
35 ralentir la vitesse d'évaporation du liquide électriquement conducteur au fur et à mesure que les gouttelettes progressent à travers la zone d'évaporation (24).
25. Procédé selon la revendication 24, dans lequel :  
le liquide électriquement conducteur est un solvant, et l'étape de ralentissement de la vitesse d'évaporation  
40 comprend la fourniture d'un écoulement gazeux à la zone d'évaporation (24), l'écoulement gazeux contenant une vapeur du solvant.
26. Procédé selon l'une quelconque des revendications 21 à 25, englobant l'étape supplémentaire consistant à :  
45 contrôler la conductivité spécifique de l'échantillon liquide, de sorte que la conductivité est située dans la plage comprise entre environ 10 micromhos/cm et environ 100 000 micromhos/cm.
27. Procédé selon la revendication 26, dans lequel le liquide électriquement conducteur renferme de l'eau et un soluté volatil ionisable.

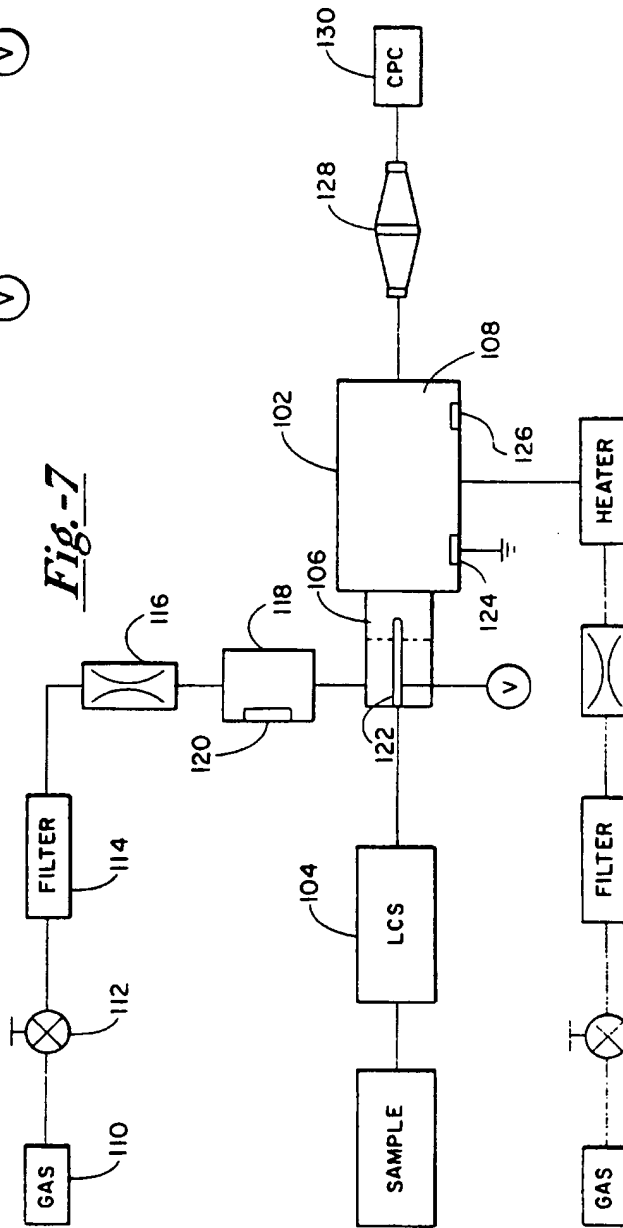
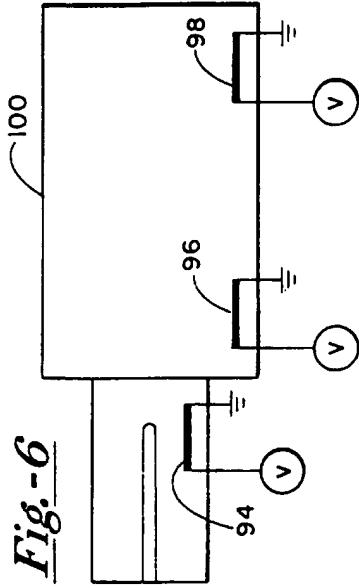
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*Fig. - 8*

